

**RESPONSE TO NON-COMPLAINT
AMENDMENT AND SUPPLEMENTAL
AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Application No. 10/729,441 (A8689)**

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1-7. (cancelled).

8. (currently amended): A composition comprising an antibody or fragment thereof, wherein said antibody or said fragment comprises at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:1-3; and wherein said light chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:4-6, and a therapeutic agent.

9-10. (cancelled).

11. (currently amended): A composition comprising an antibody or fragment thereof, wherein said antibody or said fragment comprises a heavy chain variable region, wherein said heavy chain variable region comprising the amino acid sequence of SEQ ID NO:7, and a therapeutic agent.

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12-13. (cancelled).

14. (currently amended): A composition comprising an antibody or fragment thereof, wherein said antibody or said fragment comprises a light chain variable region, wherein said light chain variable region comprising the amino acid sequence of SEQ ID NO:8, and a therapeutic agent.

15. (currently amended): A composition comprising an antibody or fragment thereof, wherein said antibody or said fragment comprises a light chain variable region comprising an amino acid sequence selected from the group consisting of:

SEQ ID NO:9;

SEQ ID NO:10;

SEQ ID NO:11; and

SEQ ID NO:12; and

wherein said composition further comprises a therapeutic agent.

16. (currently amended): A composition comprising an antibody or fragment thereof, wherein said antibody or said fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:13, and a therapeutic agent.

17. (previously presented): The composition of any one of claims 8, 11 or 14-16, wherein said therapeutic agent is selected from the group consisting of docetaxel, paclitaxel, doxorubicin, epirubicin, cyclophosphamide, trastuzumab, capecitabine, tamoxifen, toremifene,

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letrozole, anastrozole, fulvestrant, exemestane, goserelin, oxaliplatin, carboplatin, cisplatin, dexamethasone, antide, bevacizumab, 5-fluorouracil, leucovorin, levamisole, irinotecan, etoposide, topotecan, gemcitabine, vinorelbine, estramustine, mitoxantrone, abarelix, zoledronate, streptozocin, rituximab, idarubicin, busulfan, chlorambucil, fludarabine, imatinib, cytarabine, ibritumomab, tositumomab, interferon alpha-2b, melphalam, bortezomib, altretamine, asparaginase, gefitinib, erlonitib, anti-EGF receptor antibody, thalidomide, carmustine, prednisone, interferon alpha-2a, vincristine, pamidronate, erythropoietin, bisphosphonate and an epothilone.

18. (previously presented): The composition of any one of claims 8, 11 or 14-16, wherein said therapeutic agent is selected from the group consisting of carboplatin, oxaliplatin, cisplatin, paclitaxel, docetaxel, gemcitabine, and camptothecin.

19. (previously presented): A method for inhibiting the growth of a cancer cell comprising contacting said cell with the composition of claim 8.

20. (withdrawn-previously presented): A method for treating a patient having a cancer comprising administering to said patient an effective amount of the composition of claim 8.

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21. **(withdrawn-previously presented):** A method for treating a patient having a cancer comprising administering to said patient an effective amount of the pharmaceutical composition of claim 8.

22. **(previously presented):** The method of any one of claims 19-21, wherein said cancer is a cancer selected from the group consisting of breast cancer, colon cancer, ovarian carcinoma, osteosarcoma, cervical cancer, prostate cancer, lung cancer, synovial carcinoma, pancreatic cancer, melanoma, multiple myeloma, neuroblastoma, and rhabdomyosarcoma.

23. **(cancelled).**

24. **(previously presented):** A method for inhibiting the growth of a cancer cell comprising contacting a cancer cell with the composition of claim 8.

25. **(withdrawn-previously presented):** A method for treating a patient having a cancer comprising administering to said patient having a cancer an effective amount of the composition of claim 8.

26. **(previously presented):** The method of claim 24, wherein said cell is contacted with said antibody or said fragment and said therapeutic agent concurrently.

27. **(previously presented):** The method of claim 24, wherein said cell is contacted with said antibody or said fragment and said therapeutic agent sequentially and in either order.

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28. (withdrawn-previously presented): The method of claim 25, wherein said antibody or said fragment and said second therapeutic agent are administered concurrently.

29. (withdrawn-previously presented): The method of claim 25, wherein said antibody or said fragment and said second therapeutic agent are administered sequentially and in either order.

30. (previously presented): The method of claim 24 or 25, wherein said therapeutic agent is selected from the group consisting of docetaxel, paclitaxel, doxorubicin, epirubicin, cyclophosphamide, trastuzumab, capecitabine, tamoxifen, toremifene, letrozole, anastrozole, fulvestrant, exemestane, goserelin, oxaliplatin, carboplatin, cisplatin, dexamethasone, antide, bevacizumab, 5-fluorouracil, leucovorin, levamisole, irinotecan, etoposide, topotecan, gemcitabine, vinorelbine, estramustine, mitoxantrone, abarelix, zoledronate, streptozocin, rituximab, idarubicin, busulfan, chlorambucil, fludarabine, imatinib, cytarabine, ibritumomab, tositumomab, interferon alpha-2b, melphalam, bortezomib, altretamine, asparaginase, gefitinib, erlonitib, anti-EGF receptor antibody, thalidomide, carmustine, prednisone, interferon alpha-2a, vincristine, pamidronate, erythropoietin, bisphosphonate and an epothilone.

31. (previously presented): The method of claim 24 or 25, wherein said therapeutic agent is selected from the group consisting of carboplatin, oxaliplatin, cisplatin, paclitaxel, docetaxel, gemcitabine, and camptothecin.

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32. (previously presented): The composition of claim 8, wherein said therapeutic agent is selected from the group consisting of bortezomib, melphalan, thalidomide, doxorubicin, cyclophosphamide, interferon alpha-2b, interferon alpha-2a, vincristine, pamidronate, carmustine, prednisone, zoledronate, erythropoietin, bisphosphonate and dexamethasone.

33. (previously presented): The composition of any one of claims 8, 11 or 14-16, wherein said therapeutic agent is selected from the group consisting of bortezomib, melphalan, thalidomide, doxorubicin, cyclophosphamide, interferon alpha-2b, interferon alpha-2a, vincristine, pamidronate, carmustine, prednisone, zoledronate, erythropoietin, bisphosphonate and dexamethasone.

34. (previously presented): The method of claim 24 or 25, wherein said therapeutic agent is selected from the group consisting of bortezomib, melphalan, thalidomide, doxorubicin, cyclophosphamide, interferon alpha-2b, interferon alpha-2a, vincristine, pamidronate, carmustine, prednisone, zoledronate, erythropoietin, bisphosphonate and dexamethasone.

35. (withdrawn - currently amended): The method according to claim 20, wherein said effective amount of the composition of claim ~~4~~8 comprises about 1 mg/square meter to about 2000 mg/square meter of said antibody or fragment thereof, and about 10 mg/square meter to about 2000 mg/square meter of said therapeutic agent.

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36. (withdrawn - currently amended): The method according to claim 20, wherein said effective amount of the composition of claim 1-8 comprises about 10 mg/square meter to about 1000 mg/square meter of said antibody or fragment thereof, and about 50 mg/square meter to about 1000 mg/square meter of said therapeutic agent.

37. (previously presented): The composition of claim 8, wherein said antibody or said fragment is selected from the group consisting of:

- (i) a resurfaced antibody or epitope binding fragment thereof;
- (ii) a human antibody or epitope binding fragment thereof;
- (iii) a humanized antibody or epitope binding fragment thereof; and
- (iv) an antibody produced by mouse hybridoma EM164 (ATCC accession number PTA 4457) or epitope binding fragment thereof.

38. (currently amended): A composition comprising an isolated antibody or fragment thereof, wherein said antibody or said fragment comprises at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:1-3, and wherein said light chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:4-6, and wherein said antibody or said fragment specifically binds to IGF-IR; and
a therapeutic agent.

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39. (currently amended): A composition comprising an isolated antibody or fragment thereof, wherein said antibody or said fragment comprises at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises the amino acid sequence of SEQ ID NO:7, and wherein said antibody or said fragment specifically binds to IGF-IR; and
a therapeutic agent.

40. (currently amended): A composition comprising an isolated antibody or fragment thereof, comprising at least one heavy chain variable region and at least one light chain variable region, wherein said light chain variable comprises the amino acid sequence of SEQ ID NO:8; and
a therapeutic agent.

41. (currently amended): A composition comprising an antibody or antibody fragment, wherein said antibody or said fragment comprises a heavy chain variable region and a light chain variable region, wherein said heavy chain variable region comprises heavy chain complementarity-determining regions comprising the amino acid sequences of SEQ ID NOs:1-3, and wherein said light chain variable region comprises the amino acid sequence of SEQ ID NO:8; and
a therapeutic agent.

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42. (currently amended): A composition comprising an antibody or antibody fragment, wherein said antibody or said fragment comprises at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:1-3, and wherein said light chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:4-6, respectively, and wherein said heavy chain variable region comprises SEQ ID NO:7; and a therapeutic agent.

43. (currently amended): A composition comprising an antibody or fragment thereof of claim 38, comprising a light chain variable region having a sequence selected from the group consisting of:

SEQ ID NO:9,

SEQ ID NO:10,

SEQ ID NO:11 and

SEQ ID NO:12; and

wherein said composition further comprises a therapeutic agent.

44. (previously presented): A composition comprising the antibody or fragment thereof of claim 38, comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:13.

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45. (previously presented): A pharmaceutical composition comprising the antibody or antibody fragment of claim 38 and a pharmaceutically acceptable carrier.

46. (previously presented): A composition comprising a conjugate comprising the antibody or antibody fragment of claim 38 linked to a cytotoxic agent.

47. (previously presented): The composition of claim 46, wherein said cytotoxic agent is selected from the group consisting of a maytansinoid, a small drug, a prodrug, a taxoid, CC-1065 and a CC-1065 analog.

48. (previously presented): A pharmaceutical composition comprising the conjugate of claim 46 and a pharmaceutically acceptable carrier.

49. (previously presented): A composition comprising a diagnostic reagent comprising the composition of claim 45, wherein said antibody or antibody fragment is labeled with a detectable moiety.

50. (previously presented): The composition of claim 49, wherein said detectable moiety is selected from the group consisting of a radiolabel, a fluorophore, a chromophore, an imaging agent and a metal ion.

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51. (previously presented): A method for inhibiting the growth of a cancer cell comprising contacting said cell with the composition of claim 38.

52. (previously presented): A method for treating a patient having a cancer comprising administering to said patient an effective amount of the composition of claim 38.

53. (previously presented): The method of claim 52 further comprising administering to said patient a therapeutic agent.

54. (previously presented): The method of claim 53, wherein said therapeutic agent is a cytotoxic agent.

55. (previously presented): A method for treating a patient having a cancer comprising administering to said patient an effective amount of the conjugate of claim 46.

56. (previously presented): The method of treatment of claim 52, wherein said cancer is a cancer selected from the group consisting of breast cancer, colon cancer, ovarian carcinoma, osteosarcoma, cervical cancer, prostate cancer, lung cancer, synovial carcinoma and pancreatic cancer.

57. (previously presented): A method for diagnosing a subject suspect of having a cancer, said method comprising:

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administering to said subject the composition of claim 49; and

detecting the distribution of said reagent within said subject.

58. (previously presented): The method of diagnosis of claim 57, wherein said cancer is a cancer selected from the group consisting of breast cancer, colon cancer, ovarian carcinoma, osteosarcoma, cervical cancer, prostate cancer, lung cancer, synovial carcinoma and pancreatic cancer.

59. (currently amended): A composition comprising a murine antibody EM164 (ATCC deposit number PTA-4457) or a fragment thereof that specifically binds to an insulin-like growth factor-I receptor, wherein said antibody or fragment is an antagonist of said receptor and is devoid of agonist activity toward said receptor; and
a therapeutic agent.

60. (currently amended): A composition comprising a humanized or resurfaced antibody EM164 or a fragment thereof that specifically binds to an insulin-like growth factor-I receptor, wherein said antibody or fragment is an antagonist of said receptor and is devoid of agonist activity toward said receptor; and
a therapeutic agent.

61. (previously presented): The composition of claim 38, wherein said antibody or said fragment specifically binds to a human insulin-like growth factor-I receptor.

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62. (previously presented): The composition of claim 8, wherein the antibody or antibody fragment has at least one property selected from the group consisting of:

- a) inhibits cellular function of a IGF-IR without activating said IGF-IR; and
- b) inhibits tumor cell growth in the presence of serum by at least 80%.

63. (previously presented): The composition of claim 55, wherein the antibody or antibody fragment has all of said properties.

64. (currently amended): A composition comprising an isolated antibody or fragment thereof that specifically binds to IGF-IR, comprising at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises three complementarities-determining regions comprising the amino acid sequences of SEQ ID NOs:1, 54 and 3, and wherein said light chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOs:4-6; and

a therapeutic agent.

65. (currently amended): A composition comprising an antibody or fragment thereof, comprising a heavy chain variable region having a sequence selected from the group consisting of:

SEQ ID NO:39,

SEQ ID NO:40,

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SEQ ID NO:41,

SEQ ID NO:42,

SEQ ID NO:43,

SEQ ID NO: 44, and

SEQ ID NO:87; and

wherein said composition further comprises a therapeutic agent.

66. (currently amended): A composition comprising an antibody or fragment thereof, comprising a heavy chain variable region having a sequence selected from the group consisting of:

SEQ ID NO:53,

SEQ ID NO:54, and

SEQ ID NO:55; and

wherein said composition further comprises a therapeutic agent.

67. (currently amended): A composition comprising an isolated humanized antibody or epitope-binding antibody fragment that specifically binds to IGF-IR, comprising at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:1-3, respectively, and wherein said light chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:4-6; and

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a therapeutic agent.

68. (currently amended): A composition comprising an isolated humanized antibody or epitope-binding antibody fragment that specifically binds to IGF-IR, comprising at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:1-3, and wherein said light chain variable region comprising a sequence selected fro the group consisting of SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:83; SEQ ID NO:84; SEQ ID NO:85, and SEQ ID NO:86; and

a therapeutic agent.

69. (currently amended): A composition comprising an isolated humanized antibody or epitope-binding antibody fragment that specifically binds to IGF-IR, comprising at least one heavy chain variable region and at least one light chain variable region, wherein said light chain variable region comprises three complementarity-determining regions comprising the amino acid sequences of SEQ ID NOS:4-6, and wherein said heavy chain variable region comprises a sequence selected from the group consisting of SEQ ID NO:13; and SEQ ID NO:88; and

a therapeutic agent.

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70. (currently amended): A composition comprising an isolated humanized antibody or epitope-binding antibody fragment that specifically binds to IGF-IR, comprising a light chain variable region having a sequence selected from the group consisting of:

SEQ ID NO:83,

SEQ ID NO:84,

SEQ ID NO:85, and

SEQ ID NO:86; and

wherein said composition further comprises a therapeutic agent.

71. (currently amended): A composition comprising an isolated humanized antibody or epitope-binding antibody fragment that specifically binds to IGF-IR, wherein said humanized antibody or fragment comprises a heavy chain variable region having the sequence of SEQ ID NO:88; and

a therapeutic agent.

72. (currently amended): A composition comprising an antibody or fragment thereof, wherein said antibody or said fragment comprises a light chain variable region having a sequence selected from the group consisting of:

SEQ ID NO:33,

SEQ ID NO:34,

SEQ ID NO:35,

SEQ ID NO:36, and

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SEQ ID NO:37; and

wherein said composition further comprises a therapeutic agent.